RAW SEQUENCE LISTING

DATE: 02/07/2002 TIME: 13:27:56

PATENT APPLICATION: US/09/963,875

Input Set : A:\EP.txt

Output Set: N:\CRF3\02072002\I963875.raw

## ENTERED

```
3 <110> APPLICANT: Massachusetts General Hospital
     5 <120> TITLE OF INVENTION: Stem Cells of the Islets of Langerhans and Their Use in
Treating Diabetes
              Mellitus
      6
      8 <130> FILE REFERENCE: 17633/1235
C--> 10 <140> CURRENT APPLICATION NUMBER: US/09/963,875
     11 <141> CURRENT FILING DATE: 2001-09-26
     13 <150> PRIOR APPLICATION NUMBER: US60/169082
     14 <151> PRIOR FILING DATE: 1999-12-06
     16 <150> PRIOR APPLICATION NUMBER: US 60/215109
     17 <151> PRIOR FILING DATE: 2000-06-28
     19 <150> PRIOR APPLICATION NUMBER: US 60/238880
     20 <151> PRIOR FILING DATE: 2000-10-06
     22 <150> PRIOR APPLICATION NUMBER: US 09/731261
     23 <151> PRIOR FILING DATE: 2000-12-06
     25 <160> NUMBER OF SEQ ID NOS: 58
      27 <170> SOFTWARE: PatentIn version 3.1
      29 <210> SEQ ID NO: 1
      30 <211> LENGTH: 1618
      31 <212> TYPE: PRT
      32 <213> ORGANISM: Homo sapiens
      36 Met Glu Gly Cys Met Gly Glu Glu Ser Phe Gln Met Trp Glu Leu Asn
      40 Arg Arg Leu Glu Ala Tyr Leu Gly Arg Val Lys Ala Leu Glu Glu Gln
      44 Asn Glu Leu Leu Ser Ala Gly Leu Gly Gly Leu Arg Arg Gln Ser Ala
       48 Asp Thr Ser Trp Arg Ala His Ala Asp Asp Glu Leu Ala Ala Leu Arg
       52 Ala Leu Val Asp Gln Arg Trp Arg Glu Lys His Ala Ala Glu Val Ala
                                  55
       56 Arg Asp Asn Leu Ala Glu Glu Leu Glu Gly Val Ala Gly Arg Cys Glu
       60 Gln Leu Arg Leu Ala Arg Glu Arg Thr Thr Glu Glu Val Ala Arg Asn
       64 Arg Arg Ala Val Glu Ala Glu Lys Cys Ala Arg Ala Trp Leu Ser Ser
       68 Gln Gly Ala Glu Leu Glu Arg Glu Leu Glu Ala Leu Arg Val Ala His
       72 Glu Glu Glu Arg Val Gly Leu Asn Ala Gln Ala Ala Cys Ala Pro Arg
        76 Leu Pro Ala Pro Pro Arg Pro Pro Ala Pro Ala Pro Glu Val Glu
                              150
                           165
        77
```

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/963,875

DATE: 02/07/2002 TIME: 13:27:56

Input Set : A:\EP.txt

Output Set: N:\CRF3\02072002\1963875.raw

| Output Set. N. (CM2)  |
|---|
| 80 Leu Ala Arg Arg Leu Gly Glu Ala Trp Arg Gly Ala Val Arg Gly Tyr 190 185 187 188  |
| 80 Leu Ala Arg Arg Leu Gly Glu Ala 115 190  |
| 80 Leu Ara Ary 185<br>81 180 180 185<br>84 Gln Glu Arg Val Ala His Met Glu Thr Ser Leu Asp Gln Thr Arg Glu 205<br>200 205   |
| 84 Gln Glu Arg Val Ala HIS Met 310 205  |
| 84 GIN GIU AIG 195 85 195 88 Arg Leu Ala Arg Ala Val Gln Gly Ala Arg Glu Val Arg Leu Glu Leu 215 220  |
| 88 Arg Leu Ala Arg Ala var Gin  |
| 89 210 Arg Gly Gly Leu Leu Glu Arg Arg Ala Ala  |
| 88 Arg Let Mid 325  89 210  92 Gln Gln Leu Gln Ala Glu Arg Gly Gly Leu Leu Glu Arg Arg Ala Ala  240  230  231  230  235   |
| 93 225 Clu Cly Arg Trp Gln Glu Arg Leu Arg Ald Inc  |
| 93 225 230 235<br>96 Leu Glu Gln Arg Leu Glu Gly Arg Trp Gln Glu Arg Leu Arg Ala Thr<br>255<br>250 250 250 250 Cln Gly  |
| 96 Leu Glu Glu Has 245 97 100 Glu Lys Phe Gln Leu Ala Val Glu Ala Leu Glu Gln Glu Lys Gln Gly 265 260 260 260 260 260 260 260 260 260 260   |
| 100 Glu Lys Phe GIn Led Ald Val   |
| 100 Glu Lys File 260<br>101 260<br>104 Leu Gln Ser Gln Ile Ala Gln Val Leu Glu Gly Arg Gln Gln Leu Ala<br>285<br>280 285 Thr Leu  |
| 104 Leu Gln Ser Gill He Ald 280 285   |
| 104 Leu GIN Ser Leu Ser Leu Glu Val Ala Thr Tyr Arg Thr Leu 108 His Leu Lys Met Ser Leu Ser Leu Glu Val Ala Thr Tyr Arg Thr Leu 295   |
| 108 His Leu Lys Met Ser Lys 295   |
| 108 His Led Lys 130 295 300 Gly Gly Ser Lys 109 290 310 315 310 315 Gly Rho Pro Arg   |
| 112 Leu Glu Ald Glu And 310 315   |
| 112 Lett Glu Mad 310 315 315 316 317 318 319 310 411 310 315 310 Lett Glu Lett Glu Phe Pro Arg 335 330 330 331 331 331 331 331 331 331 331  |
| 116 Thr Ser Lea Ser 230 325 330 330   |
| 116 Thi Ser Box 325  117  120 Thr Pro Glu Gly Arg Arg Leu Gly Ser Leu Leu Pro Val Leu Ser Pro 350  345  345   |
| 120 Thr P10 GHz 340  121  340  124 Thr Ser Leu Pro Ser Pro Leu Pro Ala Thr Leu Glu Thr Pro Val Pro 124 Thr Ser Leu Pro Ser Pro Leu Pro Ala Thr Leu Glu Thr Pro Thr Leu                              |
| 124 mbr Ser Leu Pro Ser Pro Leu Pro Ala Thr Leu Giu 1112  |
| 124 Thi Sel 200 360 125 355 128 Ala Phe Leu Lys Asn Gln Glu Phe Leu Gln Ala Arg Thr Pro Thr Leu 375 380   |
| 129 Ala Phe Leu Lys Asn Gln Glu Phe Leu Gin Ala May 380   |
| 128 Ala File 200 17 375<br>129 370 375<br>132 Ala Ser Thr Pro Ile Pro Pro Thr Pro Gln Ala Pro Ser Pro Ala Val<br>132 Ala Ser Thr Pro Ile Pro Pro Thr Pro Gln Ala Pro Ser Pro Ala Val<br>395 400 Thr |
| 132 Ala Ser Thr Pro Ile Pro Pro Thr Pro Gin Ala 395   |
| 133 385 390 Leu Ser Leu Leu Gln Thr   |
| 415   |
| 137 405 ale Pro Glu Pro Leu Arg Ala Glu Ala Arg   |
| 136 ASP Ala Glu Ala Arg  405  137  140 Glu Pro Leu Arg Ala Glu Ala Arg  430  425  430  430  |
| 140 Gin Gly Gly 420  141  420  142 Pro Gly Pro Glu Glu Pro Gly Gly  144 Val Ala Ile Pro Ala Ser Val Leu Pro Gly Pro Glu Glu Pro Gly Gly  145  445   |
| 144 Val Ala Ile Pro Ala Ser Val Bed 145 445   |
| 144 Val Ara 125 440  145 435  148 Gln Arg Gln Glu Ala Ser Thr Gly Gln Ser Pro Glu Asp His Ala Ser  460  455   |
| 148 Gln Arg Gln Glu Ald Sel III 460 455 460   |
| 148 GH AIG GH 455  149 450  152 Leu Ala Pro Pro Leu Ser Pro Asp His Ser Ser Leu Glu Ala Lys Asp  480  470  470  |
| 152 Leu Ala Pro Pro Leu Scr 125 2 475   |
| 152 Led Ald 175 470<br>153 465 470 Led Ald 175 475<br>156 Gly Glu Ser Gly Gly Ser Arg Val Phe Ser Ile Cys Arg Gly Glu Gly<br>156 Gly Glu Ser Gly Gly 495 490 490 Ald Ile Gly Gly                    |
| 156 Gly Glu Ser Gly Gly 490   |
| 156 Gly Glu Ser Gly 485<br>157<br>160 Glu Gly Gln Ile Trp Gly Leu Val Glu Lys Glu Thr Ala Ile Glu Gly<br>505<br>505<br>508 Glu Thr Ala Ile Glu Gly Glu Asp Leu                                      |
| 160 Glu Gly Gli 110 127 505 505 505 500 Asp Leu   |
| 160 Glu Gly Glu 125 505  161 500 505  164 Lys Val Val Ser Ser Leu Gln Gln Glu Ile Trp Glu Glu Glu Asp Leu  525 520 527  |
| 164 Lys Val Val Ser   |
| 164 Lys Val Val 515  165 515  168 Asn Arg Lys Glu Ile Gln Asp Ser Gln Val Pro Leu Glu Lys Glu Thr  535 540  540 540   |
| 168 Ash Arg Lys 525 535 540 169 530 535 550 555 550 555 550 555 550 550   |
| 172 Leu Lys Ser Leu Gly Glu Glu Ile Gln Glu Ser Leu Gly 560   |
| 172 Led Lys Ser 255 550 555<br>173 545 550 550 Asn Gln Glu Cys Pro Arg<br>176 Asn Gln Ser His Glu Thr Leu Glu Arg Glu Asn Gln Glu Cys Pro Arg   |
| 176 Asn Gln Ser His Glu Thr Leu Glu Arg Glu Ash Gla   |
| 1,0 1101 0-1  |

RAW SEQUENCE LISTING

DATE: 02/07/2002 TIME: 13:27:56 PATENT APPLICATION: US/09/963,875

Input Set : A:\EP.txt

Output Set: N:\CRF3\02072002\I963875.raw

| Output Set: N:\CRF3\0207200  |
|--|
| 570  |
| 177 565 570 Leu Glu Lys Glu Asn 180 Ser Leu Glu Glu Asp Leu Glu Thr Leu Lys Ser Leu Glu Lys Glu Asn 590 585 590  |
| 100 Sor Leu Glu Glu Asp Leu Glu Thr Leu Lys Sel Leu 590  |
| 180 Ser New 580  181 580  184 Lys Arg Ala Ile Lys Gly Cys Gly Gly Ser Glu Thr Ser Arg Lys Arg  605  607  608  609  609  600  600  600  600  600  |
| 181 And Ang Ala Ile Lys Gly Cys Gly Gly Ser Glu III 502  |
| 184 Lys Alg has 505 600 The Gln The Leu  |
| 184 Lys Arg Arg Gln Leu Lys Pro Thr Gly Lys Glu Asp Thr Gln Thr Leu 188 Gly Cys Arg Gln Leu Lys Pro Thr Gly Lys Glu Asp Thr Gly Gly  |
| 188 GIY CYS AFG CAT 161 GIV GIV  |
| 188 Gly Cys May  615  189 610  192 Gln Ser Leu Gln Lys Glu Asn Gln Glu Leu Met Lys Ser Leu Glu Gly  640  630  631  |
| 192 GIn Sel Leu SIN 21 630 635 Cln Clu Leu Val   |
| 192 GIN Ser Box 630  193 625  196 Asn Leu Glu Thr Phe Leu Phe Pro Gly Thr Glu Asn Gln Glu Leu Val  655  650  650  650  650  650  |
| 196 Asn Leu Glu III III 650  |
| 196 ASR Led Glu ASR Leu Glu Ser Leu Thr Ala Leu Glu Lys Glu 197 200 Ser Ser Leu Gln Glu Asr Leu Glu Ser Leu Thr Ala Leu Glu Lys Glu 650 670 665  |
| 200 Ser Ser Leu Gill Gid Hon - 665   |
| 200 Ser Ser Leu 665 201 660 204 Asn Gln Glu Pro Leu Arg Ser Pro Glu Val Gly Asp Glu Glu Ala Leu 680 685  |
| 204 Asn Gln Glu Pro Leu Ary 502 680 685  |
| 205 6/5 The Lys Glu Ash Glu Pro Leu Arg Ser Leu Glu Asp  |
| 204 ASH GIN 625 680 .  205 675  208 Arg Pro Leu Thr Lys Glu Ash Gln Glu Pro Leu Arg Ser Leu Glu Asp  700  695  |
| 208 Arg F16 200 695 700<br>209 690 690 720<br>212 Glu Asn Lys Glu Ala Phe Arg Ser Leu Glu Lys Glu Asn Gln Glu Pro<br>710 715 720 Glu   |
| 212 Glu Asn Lys Glu Ala File 113 715 720   |
| 212 Glu ASH 270 710 713 213 705 710 710 216 Leu Lys Thr Leu Glu Glu Glu Asp Gln Ser Ile Val Arg Pro Leu Glu 735 730 736  |
| 216 Leu Lys Thr Leu Glu Glu Glu Glu Glu Glu Glu Glu Glu Gl   |
| 725 730 745 750 745 750 745 750 745 750 750 745  |
| 220 Thr Glu Asn His Lys Ser Lett May 745   |
| 745 221 740 745 221 Thr Leu Arg Thr Leu Glu Lys Glu Thr Gln Gln Arg Arg Arg Ser Leu 760 760 760 761 762  |
| 224 Thr Leu Arg Thr Leu Glu Lys Glu 112 765  |
| 224 Thi Bed 175 760 225 755 760 228 Gly Glu Gln Asp Gln Met Thr Leu Arg Pro Pro Glu Lys Val Asp Leu 775 780  |
| 228 Gly Glu Gln Asp Gin Met illi Hed May 780   |
| 229 770 7/3 Cln Clu Tle Ala Arg Pro Leu Glu Ash  |
| 229 770 775 775 776 229 770 Leu Glu Asn 232 Glu Pro Leu Lys Ser Leu Asp Gln Glu Ile Ala Arg Pro Leu Glu Asn 790 795 790 791 Glu Ala  |
| 232 Glu Flo Zee -1 790 795 233 785 790 236 Glu Asn Gln Glu Phe Leu Lys Ser Leu Lys Glu Glu Ser Val Glu Ala 815 810 805   |
| 236 Glu Asn Gln Glu Phe Leu Lys Ser Hed 27   |
| 237 805 Ser Leu Lys Ser Ala Gly  |
| 236 Glu Ash Glu 805<br>805<br>237 805 810 Ser Leu Lys Ser Ala Gly<br>240 Val Lys Ser Leu Glu Thr Glu Ile Leu Glu Ser Leu Lys Ser Ala Gly<br>830  |
| 241 820 Fro Glu Thr Gln Ala Pro Leu  |
| 240 Val Lys 820 825<br>241 820 Ser Pro Glu Thr Gln Ala Pro Leu<br>244 Gln Glu Asn Leu Glu Thr Leu Lys Ser Pro Glu Thr Gln Ala Pro Leu<br>845 846 847   |
| 244 GIN GIU ASN 255 840 840 245 835 840 248 Trp Thr Pro Glu Glu Ile Asn Lys Ser Gly Gly Asn Glu Ser Ser Arg 860 855 860 875 Arg Asp  |
| 248 Trp Thr Pro Glu Glu Ile Ash Lys Sel Gly 327  |
| 248 TIP THE 120 855 249 850 855 252 Lys Gly Asn Ser Arg Thr Thr Gly Val Cys Gly Ser Glu Pro Arg Asp 880 875 870 875  |
| 252 Lys Gly Asn Ser Arg Thr Thr Gly Val Cys 875  |
| 252 Lys Gly ABB 870 875 253 865 870 885 890 895 885 890 885 Republic Ser Gly Arg Gly A |
| 256 Tle Gln Thr Pro Gly Arg Gly Glu Ser Gly 110 120 895  |
| 256 The GIM 257<br>885<br>257<br>260 Ser Met Glu Pro Gly Glu Phe Glu Ile Ser Arg Gly Val Asp Lys Glu<br>910<br>905<br>910 Tyr  |
| 250 Ser Met Glu Pro Gly Glu Phe Glu IIe Ser Ary Gri 910  |
| 905 900 900 Ton Cly Lys Gly Glu Tyr  |
| 260 Sel Met Glu 900<br>261 900<br>264 Ser Gln Arg Asn Leu Glu Glu Glu Glu Asn Leu Gly Lys Gly Glu Tyr<br>925<br>920 925  |
| 264 Ser Gin Aly 1151 920 920   |
| 265 915 920 920 920 920 940 935 940 935  |
| 268 Gin Giu Sei Bed and 935 935 935  |
| 269 930 935<br>272 Ser Ala Asp Val Gln Arg Trp Glu Asp Thr Val Glu Lys Asp Gln Glu<br>950 955  |
| 272 Ser Ala Asp 142 950  |
| 273 945  |
|  |

DATE: 02/07/2002 RAW SEQUENCE LISTING TIME: 13:27:56 PATENT APPLICATION: US/09/963,875

Input Set : A:\EP.txt

Output Set: N:\CRF3\02072002\1963875.raw

```
276 Leu Ala Gln Glu Ser Pro Pro Gly Met Ala Gly Val Glu Asn Lys Asp
280 Glu Ala Glu Leu Asn Leu Arg Glu Gln Asp Gly Phe Thr Gly Lys Glu
284 Glu Val Val Glu Gln Gly Glu Leu Asn Ala Thr Glu Glu Val Trp Phe
288 Pro Gly Glu Gly His Pro Glu Asn Pro Glu Pro Lys Glu Gln Arg
                               1000
292 Gly Leu Val Glu Gly Ala Ser Val Lys Gly Gly Ala Glu Gly Leu
296 Gln Asp Pro Glu Gly Gln Ser Gln Gln Val Gly Thr Pro Gly Leu
 300 Gln Ala Pro Gln Gly Leu Pro Glu Ala Ile Glu Pro Leu Val Glu
 304 Asp Asp Val Ala Pro Gly Gly Asp Gln Ala Ser Pro Glu Val Met
 308 Leu Gly Ser Glu Pro Ala Met Gly Glu Ser Ala Ala Gly Ala Glu
                             1075
 312 Pro Gly Leu Gly Gln Gly Val Gly Gly Leu Gly Asp Pro Gly His
                             1090
 316 Leu Thr Arg Glu Glu Val Met Glu Pro Pro Leu Glu Glu Glu Ser
 320 Leu Glu Ala Lys Arg Val Gln Gly Leu Glu Gly Pro Arg Lys Asp
                             1120
 324 Leu Glu Glu Ala Gly Gly Leu Gly Thr Glu Phe Ser Glu Leu Pro
  328 Gly Lys Ser Arg Asp Pro Trp Glu Pro Pro Arg Glu Gly Arg Glu
                              1150
  332 Glu Ser Glu Ala Glu Ala Pro Arg Gly Ala Glu Glu Ala Phe Pro
                              1165
  336 Ala Glu Thr Leu Gly His Thr Gly Ser Asp Ala Pro Ser Pro Trp
                              1180
  340 Pro Leu Gly Ser Glu Glu Ala Glu Glu Asp Val Pro Pro Val Leu
                              1195
  344 Val Ser Pro Ser Pro Thr Tyr Thr Pro Ile Leu Glu Asp Ala Pro
                              1210
  348 Gly Leu Gln Pro Gln Ala Glu Gly Ser Gln Glu Ala Ser Trp Gly
   352 Val Gln Gly Arg Ala Glu Ala Gly Lys Val Glu Ser Glu Gln Glu
   356 Glu Leu Gly Ser Gly Glu Ile Pro Glu Gly Leu Gln Glu Gly Gly
   360 Glu Glu Ser Arg Glu Glu Ser Glu Glu Asp Glu Leu Gly Glu Thr
   364 Leu Pro Asp Ser Thr Pro Leu Gly Phe Tyr Leu Arg Ser Pro Thr
                               1285
   368 Ser Pro Arg Trp Thr Pro Leu Glu Ser Arg Gly His Pro Leu Lys
   372 Glu Thr Gly Lys Glu Gly Trp Asp Pro Ala Val Leu Ala Ser Glu
```

DATE: 02/07/2002 RAW SEQUENCE LISTING TIME: 13:27:56 PATENT APPLICATION: US/09/963,875

Input Set : A:\EP.txt

Output Set: N:\CRF3\02072002\1963875.raw

```
1330
376 Gly Leu Glu Glu Pro Ser Glu Lys Glu Glu Gly Glu Gly Glu
380 Glu Glu Cys Gly Arg Asp Ser Asp Leu Ser Glu Glu Phe Glu Asp
                            1345
                            1360
384 Leu Gly Thr Glu Ala Pro Phe Leu Pro Gly Val Pro Gly Glu Val
                            1375
388 Ala Glu Pro Leu Gly Gln Val Pro Gln Leu Leu Asp Pro Ala
                            1390
392 Ala Trp Asp Arg Asp Gly Glu Ser Asp Gly Phe Ala Asp Glu Glu
396 Glu Ser Gly Glu Glu Glu Glu Glu Glu Glu Gly Arg Glu
                             1405
                            1420
400 Pro Gly Ala Gly Arg Trp Gly Pro Gly Ser Ser Val Gly Ser Leu
 404 Gln Ala Leu Ser Ser Ser Gln Arg Gly Glu Phe Leu Glu Ser Asp
                             1435
                             1450
 408 Ser Val Ser Val Ser Val Pro Trp Asp Asp Ser Leu Arg Gly Ala
 405
 412 Val Ala Gly Ala Pro Lys Thr Ala Leu Glu Thr Glu Ser Gln Asp
                             1465
                             1480
 416 Ser Ala Glu Pro Ser Gly Ser Glu Glu Glu Ser Asp
                                                      Pro Val Ser
 413
                                                  1500
                             1495
 420 Leu Glu Arg Glu Asp Lys Val Pro Gly Pro Leu Glu Ile Pro Ser
                              1510
 424 Gly Met Glu Asp Ala Gly Pro Gly Ala Asp Ile Ile
                                                       Gly Val Asn
 428 Gly Gln Gly Pro Asn Leu Glu Gly Lys Ser Gln His Val Asn Gly
                              1525
 425
  432 Gly Val Met Asn Gly Leu Glu Gln Ser Glu Glu Ser Gly Ala Arg
                              1540
                              1555
  436 Asn Ala Leu Val Ser Glu Gly Asp Arg Gly Ser Pro Phe Gln Glu
                              1570
  440 Glu Glu Gly Ser Ala Leu Lys Arg Ser Ser Ala Gly Ala Pro Val
  444 His Leu Gly Gln Gly Gln Phe Leu Lys Phe Thr Gln Arg Glu Gly
                              1585
                              1600
          1595
  448 Asp Arg Glu Ser Trp Ser Ser Gly Glu Asp
                              1615
          1610
  449
  452 <210> SEQ ID NO: 2
  453 <211> LENGTH: 4854
  454 <212> TYPE: DNA
  455 <213> ORGANISM: Homo sapiens
   458 atggaggget geatggggga ggagtegttt eagatgtggg ageteaateg gegeetggag
                                                                           60
   460 gcctacctgg gccgggtcaa ggcgctggag gagcagaatg agctgctcag cgccggactc
                                                                          120
   462 gggggggctcc ggcgacaatc cgcggacacc tcctggcggg cgcatgccga cgacgagctg
                                                                          180
   464 geggeeetge gtgegetegt tgaccaaege tggegggaga ageaegegge egaggtggeg
                                                                          240
   466 cgcgacaacc tggctgaaga gctggagggc gtggcaggcc gatgcgagca gctgcggctg
                                                                          300
```

VERIFICATION SUMMARY

PATENT APPLICATION: US/09/963,875

DATE: 02/07/2002 TIME: 13:27:57

Input Set : A:\EP.txt
Output Set: N:\CRF3\02072002\I963875.raw

L:10 M:270 C: Current Application Number differs, Replaced Current Application Number